Transgender Health
Volume 7, Number 4, 2022
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DOI: 10.1089/trgh.2021.0006

SHORT REPORT

Transgender Youth Experiences with Implantable GnRH Agonists for Puberty Suppression

Brianna J. Hobson,[1,*] Elle Lett,[2,3] Linda A. Hawkins,[4] Robert A. Swendiman,[5] Michael L. Nance,[6] and Nadia L. Dowshen[7]

Abstract

This descriptive study reports caregiver experiences with GnRH agonist implants among a cohort of youth followed in a pediatric hospital-based gender clinic. We administered a survey to 36 of 55 eligible caregivers ascertaining demographics and satisfaction, with a medical record review of any surgical complications. The overwhelming majority (97.1%) reported satisfaction with the procedure and would undergo the implant procedure again (94.4%). The most frequent challenges noted were about affordability (39.8%) and insurance denials (39.8%). Implantable GnRH agonist can be used successfully in pediatric patients with gender dysphoria. Future policy should seek to address concerns regarding insurance approval and reimbursement.

Keywords: implant; insurance; patient satisfaction; puberty blockers; transgender youth

Introduction

Transgender is an umbrella term including many gender identities of individuals who do not identify with their sex assigned at birth.[1] Many children who are transgender experience significant distress with the differences between their body and their gender identity, receiving the diagnosis of gender dysphoria.[2] For transgender children, pubertal suppression with a GnRH agonist is recommended to prevent the development of unwanted secondary sex characteristics that do not align with their gender identity.[3–5] These medications have been shown to reduce depression and suicidality when prescribed for transgender children and have been shown to be safe in both children who are transgender and those who have received treatment for central precocious puberty.[6]

GnRH agonists used for pubertal suppression come in a variety of forms, including injectables that come in monthly, every 3 month, or every 6 month depot forms or a subcutaneous implant that may be effective in suppressing puberty for 1–2 years (Supprelin©; Endo Pharmaceuticals, Westbury, NY).[7,8] Studies have determined the histrelin implant to be an effective and safe alternative including a limited population of transgender patients.[7,9–11] Supprelin is the only implant that is approved for children under 18 and received its indication for central precocious puberty. There are some potential advantages for use of the implant among transgender children, including that the implant avoids the needs for regular injections and visits to a health care provider to administer the injections.[8,11,12]

Although puberty blockers are shown to be associated with positive medical and psychosocial outcomes for transgender youth, there have been no reports on outcomes of the procedure itself and parents' perceptions of the process.[6,13] The aim of this study was to determine the surgical outcomes and parent satisfaction with histrelin implant procedure among a cohort of youth followed in a large pediatric hospital-based gender clinic.

[1]Institute for Graduate Clinical Psychology, Widener University, Chester, Pennsylvania, USA.
[2]Leonard Davis Institute for Health Economics, University of Pennsylvania, Philadelphia, Pennsylvania, USA.
[3]Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA.
[4]Gender & Sexuality Development Program, The Children's Hospital of Philadelphia, Pennsylvania, USA.
[5]Department of Surgery, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA.
[6]Division of Pediatric General, Thoracic and Fetal Surgery, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA.
[7]Children's Hospital of Philadelphia, Philadelphia, Pennsylvania and Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

*Address correspondence to: Brianna Hobson, MA, Institute for Graduate Clinical Psychology, Widener University, One University Place, Chester, PA 19013, USA, E-mail: bjhobson@widener.edu

Materials and Methods

This study included a survey of parents of children who had the implant procedure and subsequent medical record review. Potential participants included parents/caregivers of all children undergoing histrelin implantation, replacement, or removal for the diagnosis of gender dysphoria between January 1, 2008 and May 31, 2019 at the Children's Hospital of Philadelphia Gender and Sexuality Development Clinic. This study was approved by the Institutional Review Board at the Children's Hospital of Philadelphia.

Medical record review

For all participants who completed the survey, their child's medical record was reviewed and the following variables were extracted: the child's demographics (age, gender, race, and ethnicity) and clinical data (height, weight, body mass index, other medical diagnoses, and medications). Procedure reports and surgery office notes were reviewed to determine the procedure type (initial insertion, replacement, and terminal removal), procedure location (outpatient clinic and sedation unit) and reported complications.

All statistical analyses were performed in R Version 4.0.2. Descriptive statistics are presented as means (SD) and medians (interquartile range) for parametric and nonparametric data, respectively. Content analysis was performed for open-ended survey responses that were double coded and categorized by theme.

Survey

Eligible subjects ($n = 55$) were identified through the electronic medical record (EMR). A total of 55 eligible patient-families were identified. From February 2019 to May 2019 eligible participants were contacted by phone up to five times to invite their participation in the study. If potential subjects were reached, the caregivers were introduced to the study and verbal consent was obtained. Participants were given the option to complete the survey over the phone or through a REDCap e-mail link. Survey questions included Likert scales, closed ended and open-ended prompts to ask subjects about their child's transition, the insurance process, expectations and satisfaction with the surgical procedure, and any worries and improvements regarding the implant pre- and postprocedure (Supplementary Appendix).

Results

Of the 55 eligible subjects, 36 (65.5%) agreed to participate in the study. These subjects' children had original procedure dates between January 2008 and 2019. The median age at insertion was 11.50 (interquartile range: 11–13). Youth were predominantly white (83.3%) and assigned female at birth (58.3%). The time from diagnosis of gender dysphoria to implantation was < 2 years for more than half (52.7%) of patients (Table 1). One patient had used injectable GnRH medication before implant insertion.

The procedure was performed in the outpatient clinic in 32 patients (88.9%) and outpatient sedation unit in the remainder (4 patients, 11.1%). The preferred setting for implantation is the outpatient clinic under a local anesthetic. This location is chosen by the vast majority of patients and families. In certain circumstances, for example, extreme procedural anxiety, the procedure was performed in the sedation unit at the request of the family. Complications of the procedure were reported in two patients (5.6%) and included a spitting suture requiring no treatment and one case with a failure to suppress requiring resumption of injectable GnRH

Table 1. Respondent Demographics and Procedure Timeline ($N = 36$)

Variable	Distribution
Demographics	
Age at insertion, median (IQR)	11.50 (11–13)
Gender, *N* (%)	
Assigned female at birth	21 (58.3)
Assigned male at birth	15 (41.7)
Race, *N* (%)	
Asian	1 (2.8)
Black	1 (2.8)
White	30 (83.3)
Other	4 (11.1)
Ethnicity, *N* (%)	
Hispanic or Latino	0 (0)
Non-Hispanic or Latino	36 (100.0)
Procedure information and timeline	
Procedure location	
Outpatient	32 (88.9)
Sedation unit	4 (11.1)
Time from procedure to survey, *N* (%)	
0–6 months	9 (25.0)
12–18 months	8 (22.2)
18–24 months	5 (13.9)
6–12 months	8 (22.2)
> 2 years	5 (13.9)
Missing	1 (2.8)
Time from diagnosis to implant, *N* (%)	
< 1 year	3 (8.3)
1–2 years	16 (44.4)
3–4 years	9 (25.0)
≥ 5 years	7 (19.4)
Missing	1 (2.8)
Time until resumption of normal activity, *N* (%)	
< 1 day	21 (58.3)
1–3 days	12 (33.3)
3–5 days	2 (5.6)
> 1 week	1 (2.8)

agonist. Almost all patients (91.6%) reported resumption of normal activities within 3 days of the procedure.

The survey was completed by a parent/caregiver of 36 patients (12 by phone and 24 online). The most common time between when caregivers came to understand their child as transgender and survey completion was 1–2 years (44.4%) (Table 1). According to parents, the procedure process met expectations in 34 of 35 (97.1%, one missing value) patients and 34 of 36 (94.4%) would choose an implant again. Among caregivers, 58.3% noted little or no worry before their child receiving the implant, and 86.1% noted little or no worry after receiving the implant. Similarly, they noted that 44.4% of their children experience little or no worry before receiving the implant, and 86.1% reported little or no worry after receiving the implant. All but one participant was very satisfied or extremely satisfied with the cosmetic outcome and all were very satisfied or extremely satisfied with the procedure itself (Table 2).

Insurance approval-related issues were common and reported by 86.1% of families. The most common obstacles faced surrounding the approval process were insurance denial (38.9%), concerns regarding ability of affording the procedure (38.9%), and caregiver stress related to the approval process (30.6%) (Fig. 1).

Table 2. Survey Item Likert Responses, Dichotomized at 4 or Greater

Item	Count (%)
On a scale of 1–5 (1 = extremely hard and 5 = extremely easy), please rate your overall experience with insurance approval for the implant.	22 (61.1)
On a scale of 1–5 (1 = not satisfied and 5 = extremely satisfied), please rate your overall SATISFACTION with the implant procedure (putting the implant into the arm).	36 (100.0)
On a scale of 1–5 (1 = not satisfied and 5 = extremely satisfied), please rate your overall SATISFACTION with the cosmetic appearance of your child's incisions (putting the implant into the arm)?	35 (97.2)
On a scale of 1–5 (1 = extreme discomfort and 5 = no discomfort), please rate your overall DISCOMFORT with the procedure.	25 (69.4)
On a scale of 1–5 (1 = extremely daily worry and 5 = no worry), how would you rate *your* worry about the implant before receiving the implant?	21 (58.3)
On a scale of 1–5 (1 = extremely daily worry and 5 = no worry) how would you rate *your child's* worry about the implant before receiving the implant?	16 (44.4)
On a scale of 1–5 (1 = extremely daily worry and 5 = no worry) how would you rate *your* worry since receiving the implant?	31 (86.1)
On a scale of 1–5 (1 = extremely daily worry and 5 = no worry) how would you rate *your child's* worry since receiving the implant?	31 (86.1)

Several themes were reported in the parent's responses to open-ended survey questions. Overall, parents reported having a positive experience and process with the surgery and clinical staff. The most commonly reported concerns were before the procedure. Most parents again reported worrying about financial concerns, particularly regarding insurance coverage, and parents reported believing their children were most worried about pain and timing with puberty. In stark contrast, the responses regarding concerns after the procedure showed less worry for parents and their children. Most parents reported for themselves and their children that there were no concerns or downsides to the implant procedure. In fact, when reflecting on any improvements since the procedure most reported for themselves and their children relief from their transgender child not needing to start natal puberty.

Few parents reported a downside or worry for themselves and their children, most commonly related to complications, side effects (e.g., ineffective and rejection), efficacy of the implant, how long the effects of the implant would last, and the impact on their children's well-being and development.

Discussion

Overall, these data show high rates of caregiver satisfaction with the histrelin implant procedure and willingness to undergo the procedure again for their children with gender dysphoria. Furthermore, there were no serious complications that could not be easily remediated, almost all children returned to normal function within 3 days of the procedure, and parents reported decreased worry for both them and their children after the procedure.

The high satisfaction ratings and low rates of surgical complications with the histrelin implant procedure evidenced in our study was similar to those among children with central precocious puberty (CPP).[10] A large majority of the parents in our study stated that they would agree for their children undergo surgical implantation procedure again (97.1%)—slightly higher than the percentage for parents of children with CPP (95%). Regarding low rates of complications, only three cases during implant removal for children with CPP were reported. Our study reported only two cases that were easily resolved and did not require any additional treatment, which suggest complications are rare and easily remedied. Also of note, children in our study were older on average than those who received histrelin implants for CPP, and our data suggest that the procedure is similarly well tolerated in youth with gender dysphoria in early adolescence.

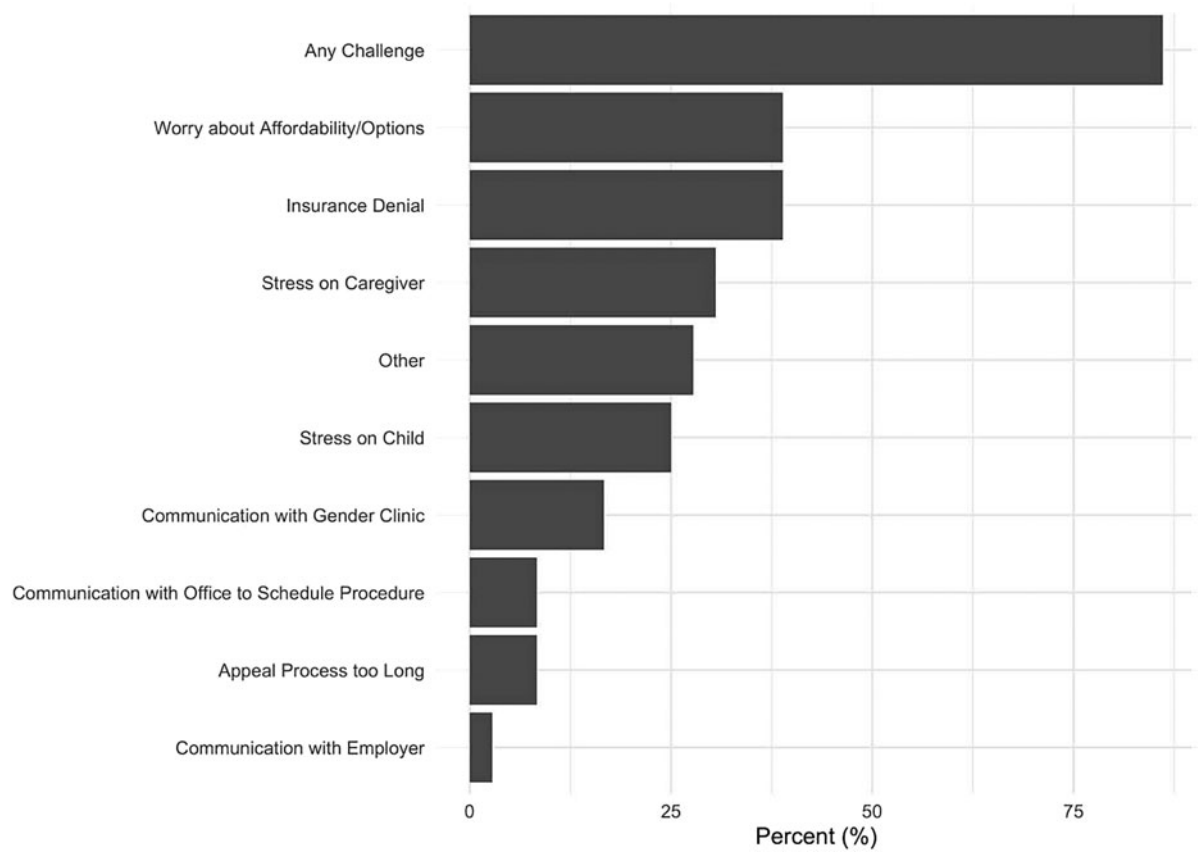

FIG. 1. Challenges with the GnRH agonist implant process reported by caregivers ($n = 36$).

Interestingly, the only major concern from parents was not actually procedure related, but rather frustration with the insurance approval process, including affordability of the procedure and insurance denial. This finding further reinforces, as has been shown in other studies, that insurance approval, lack of transparency regarding coverage, and high cost of blockers is a major concern to youth, parents, and providers.[14,15] As noted in a commentary in *Pediatrics* in 2015,[14] over time insurance companies have been more willing to approve GnRH agonists for children with gender dysphoria, but the process may take significant time—now 2 to 4 weeks (some can take 2–3 months) weeks on average in our clinic—leading to additional time of unnecessary dysphoria and distress for children and parents. Although this study adds to emerging literature on the success of pubertal suppression in youth with gender dysphoria, addressing concerns around processes for approval and related delays in insurance approvals will be critical to improving patient-centered outcomes.[3,5,6,13,16]

The study has several limitations. The data were obtained retrospectively from caregivers, which may have influenced their responses to the survey questions.[17] Also obtaining data from the caregivers' perspective may have influence and place assumptions on the direct experience transgender children with gender dysphoria. This study also follows histrelin implantation in majority white non-Hispanic patients, which highlights the racial disparity in access to medically appropriate gender-affirming care and impacts generalizability.[18,19] Future research will assist in validating these findings, including studies with a larger sample size, with a more diverse sample population, using a prospective study design, and obtaining data directly from the transgender child perspective.

Conclusions

Our study is one of the first to examine the experience of the process for GnRH agonist implantation for children with gender dysphoria from the parent

perspective. We demonstrate high satisfaction among caregivers with the procedure and willingness to have their child undergo the procedure again. Future research and policy should examine how experiences compare between those who receive injectable GnRH agonists and address the most common challenges reported by caregivers related to insurance approval.

Acknowledgment

We thank the clinical and research staff of the CHOP GSDC and our patients and their caregivers for participating in this study.

Authors' Contributions

B.H. (primary author) contacted patients, collected and analyzed data, and contributed toward the article and study design. E.L. analyzed data, compiled all tables and figures, wrote the abstract, and edited and revised the article. L.H. contributed toward study design, data analysis, and revision to the article and abstract. R.A.S. designed the study and contributed toward data analysis, literature review, and revision to the abstract and article. M.L.N. conceived the idea of the study and contributed toward study design, data analysis, and revision to the abstract and article. N.D. (senior author) contributed toward study design, literature review, data analysis, and critical revisions to the article.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

This research study was funded by the Children's Hospital of Philadelphia (CHOP). This project was also supported in part by a grant to Dr. Dowshen from the Stoneleigh Foundation.

Supplementary Material

Supplementary Appendix

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Cite this article as: Hobson BJ, Lett E, Hawkins LA, Swendiman RA, Nance ML, Dowshen NL (2022) Transgender youth experiences with implantable GnRH agonists for puberty suppression, *Transgender Health* 7:4, 364–368, DOI: 10.1089/trgh.2021.0006.

Abbreviation Used

CPP = central precocious puberty